

Influenza vaccine segment from Immunization Update satellite broadcast, August 15, 2002

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In this segment of the program we want to discuss this year's influenza vaccine recommendations. As you know, ACIP updates its influenza vaccine recommendations every year. This year's ACIP statement was published in April 2002. The most significant changes in this year's recommendations are the timing of influenza vaccination by risk group; the 2002- 2003 vaccine virus strains; the availability of certain influenza vaccine doses with reduced thimerosal content, and influenza vaccine for children aged 6 to 23 months of age. We will discuss the first 3 issues briefly, and the new pediatric vaccination recommendation in more detail.

In the United States and other temperate areas of the northern hemisphere, influenza occurs most commonly between December and March. The optimum time to vaccinate is usually during October and November. As you are aware, there have been substantial delays in the distribution of influenza vaccine during the last two years. Influenza vaccine production is complex, and it is possible that delays in distribution could occur again.

To minimize disruptions caused by these delays, ACIP now recommends that providers focus their vaccination efforts in October and earlier on persons at high risk of complications of influenza and their household contacts, and health-care workers. Vaccination of children 6 months to 9 years of age who are receiving vaccine for the first time should also begin in October because they need a second dose 1 month after the first. Vaccination of all other groups should begin in November, including healthy people aged 50 to 64 years, and other people who wish to reduce their risk for influenza infection.

Vaccine should be offered to people at increased risk of complications of influenza when they access medical care in September, if vaccine is available. Vaccination of high risk persons early is easier if offices have a reminder and recall system in place.

Here are the groups at high risk of complications of influenza. First and foremost, all persons 65 years of age or older, and persons 6 months of age and older with any of a

variety of chronic illnesses should be vaccinated. Healthy children 6 to 23 months of age are at increased risk of complications of influenza - we will discuss vaccination of this group in more detail in a few minutes.

The chronic illnesses that increase the risk of influenza complications include: pulmonary diseases such as emphysema and asthma; cardiovascular diseases; and metabolic diseases like diabetes. Additionally, renal dysfunction, like chronic renal failure or nephropathy; hemoglobinopathies, like sickle cell disease; and immunosuppression, including HIV, are high risk conditions. In addition to seniors and people with chronic illnesses, other risk groups include residents of long term care facilities, and persons 6 months to 18 years of age receiving chronic aspirin therapy, because of the risk of Reyes. Finally, most pregnant women are recommended to be routinely vaccinated- specifically those who will be in the second or third trimester of pregnancy during influenza season.

Health care workers are at increased risk of exposure to influenza. Also, a health care worker with influenza could expose many of his or her patients who are at high risk of complications of influenza. So health care workers are a high priority for early supplies of influenza vaccine. Yet in 2000, only about 38 percent of health care workers reported having been vaccinated in the previous year. Health care workers- ALL health care workers- owe it to their patients to receive annual influenza vaccine, and to receive it early in the season.

There seems to be a perception that influenza vaccination is an October activity. It's been difficult to convince providers to continue providing vaccine to their patients into December and beyond. It's critical that we change this perception.

This graph shows the month in which influenza activity peaked in the United States from 1976 through 2001. Influenza activity peaked in December in only 16 percent of seasons. Activity peaked in January in 24 percent of seasons and in February in 40 percent of seasons. The message here is that December is NOT too late to receive influenza vaccine. Vaccination in January or even February can still prevent a lot of influenza.

ACIP recommends that providers should continue to offer influenza vaccine to their patients, especially those at high risk of complications, and to health care workers in December. Providers should continue to vaccinate throughout influenza

season as long as vaccine is available, even after influenza activity has been documented in the community.

The influenza vaccines available in the U.S. are inactivated subunit vaccines. The two types of subunit vaccine available contain either split virus, or purified hemagglutinin. The whole inactivated virus vaccine is no longer available in this country. Available influenza vaccines are trivalent- meaning they contain 3 different viruses, two type A viruses and one type B. The viruses contained in the vaccine are chosen each spring, based on surveillance of current circulating strains. Only the B virus component was changed this year.

The vaccine recommended for the 2002- 2003 season includes A/Moscow/10/99- the H3N2 strain; A/New Caledonia/20/99- the H1N1 strain, and B/Hong Kong/ 330/2001. For the A/Moscow antigen, manufacturers will use the antigenically equivalent A/Panama/2007/99 strain. A different, antigenically equivalent B strain may be substituted for the B/Hong Kong antigen. These substitute viruses will be used because of their growth properties, and because they are representative of influenza viruses likely to circulate in the United States during the 2002- 2003 influenza season.

Influenza vaccine is made from highly purified, egg-grown viruses that have been made noninfectious. Because the vaccine viruses are initially grown in embryonated hens' eggs, the vaccine might contain a small amount of residual egg protein. Consequently, this vaccine should not be used, or used with extreme caution, among persons with anaphylactic egg allergy.

Influenza vaccine distributed in the United States also contains thimerosal, a mercury- containing compound, as the preservative. Thimerosal has been used as a preservative in vaccines since the 1930s. There is no evidence of harm caused by thimerosal in vaccines. But in 1999, the U.S. Public Health Service and other organizations recommended that efforts be made to reduce the thimerosal content in vaccines to decrease total mercury exposure, chiefly among infants and pregnant women. Since mid- 2001, all routinely administered childhood vaccines for the U.S. market have been manufactured either without thimerosal, or with only trace amounts of thimerosal. This has resulted in a substantial reduction in the total mercury exposure from vaccines for children.

For the 2002- 2003 influenza season, a limited number of doses of reduced thimerosal- content influenza vaccine will be available. Currently, reduced thimerosal content vaccine is

available from only one manufacturer, Evans Vaccines, marketed with the trade name Fluvirin. Fluvirin contains less than 1 microgram of thimerosal per dose, compared to 25 micrograms per dose for other influenza vaccines. Fluvirin is approved for use in persons 4 years of age and older. It should NOT be used in children 6 months to 4 years of age.

ACIP believes that because of the known risks for severe illness from influenza infection and the benefits of vaccination, the benefit of influenza vaccine with reduced or standard thimerosal content outweighs the theoretical risk, if any, from thimerosal. The removal of thimerosal from other vaccines further reduces the theoretical risk from thimerosal in influenza vaccines.

Another addition to this year's influenza recommendations is a discussion of vaccination of healthy children. Influenza is a common cause of respiratory illness among children. Rates of hospitalization among children less than 24 months of age are as high as rates among seniors.

After much discussion, ACIP is taking the first steps toward what will eventually be the routine annual influenza vaccination of ALL children 6 to 23 months of age.

We asked Dr. Carolyn Bridges, a medical epidemiologist in CDC's Influenza Branch, and Dr. Bonnie Word, chair of ACIP's influenza working group, to talk to us about the impact of influenza in children, and ACIP's new recommendations.

DR. CAROLYN BRIDGES:

Influenza is an acute infectious disease caused by the influenza virus. Epidemics of influenza typically occur during the winter months in the United States and other temperate areas of the northern hemisphere. During these annual winter epidemics in the United States, 10%-20% of the population may be affected. Complications of influenza are mostly respiratory, and include primary influenza pneumonia and secondary bacterial pneumonia, often caused by *Streptococcus pneumoniae*, or pneumococcus and other bacteria. Influenza can also cause worsening of underlying illnesses, such as congestive heart failure and diabetes.

Infection with influenza virus can be fatal. Influenza-related deaths can result from pneumonia as well as from exacerbations of cardiopulmonary conditions and other chronic diseases. An average of approximately 20 thousand influenza-associated deaths occur each year in the United States, with more than 40

thousand deaths in some years. Persons 65 years of age and older account for more than 90% of these deaths. In the United States, pneumonia and influenza deaths may be increasing in part because the number of older persons is increasing.

Influenza is also a common cause of hospitalization. During the past 30 years, the estimated overall number of influenza-associated hospitalizations in the United States ranged from 16,000 to 220,000 per epidemic with an average of 114,000. While persons 65 years of age and older account for more than 90% of influenza-related DEATHS, this age group accounts for about 43% of influenza-related hospitalizations. Groups traditionally considered at increased risk of complications of influenza include persons 65 years of age and older, and persons of any age with underlying illness, such heart or lung disease, diabetes, renal failure, or immune suppression. Healthy women in the second and third trimesters of pregnancy are also at risk of complications compared to women of the same age who are not pregnant. Studies also indicate that rates of influenza-related hospitalization are higher among young children compared with older children.

The interpretation of increased hospitalization rates among children during the winter has been difficult because of the co-circulation of influenza and respiratory syncytial viruses, or RSV. RSV is also a cause of serious respiratory illness among children during the winter. Recent studies have attempted to separate the effects of RSV and influenza virus. This table summarizes age-specific rates of influenza related hospitalizations per 100 thousand population from several published studies. The rates among people with high risk medical conditions B such as underlying heart or lung disease- are shown in the center column, and those without high risk conditions in the right column. In these studies, children zero to 4 years of age- shown in the first row- had rates of hospitalization higher than any other age group through age 64. The hospitalization rate among children zero to 4 years with high risk medical conditions was 500 per 100 thousand population, 5 times higher than healthy children of the same age. This rate of hospitalization was higher than any other age group with high-risk conditions through age 64. In some studies the hospitalization rate among young children with high-risk medical conditions was even higher than among people 65 years and older.

The risk of complications and hospitalization is not equal for all children. This table shows rates of influenza related

hospitalizations by age of a medicaid population in Tennessee. By far the highest rates of hospitalization were among children 11 months of age and younger, particularly those with high-risk medical conditions, shown in the center column. But rates of hospitalization were also very high through 2 years of age in both healthy children and those with high-risk conditions. Rates of hospitalization in HEALTHY children 2 years of age and younger were higher than rates among older children with high risk underlying medical conditions- groups for which influenza vaccine has been recommended for many years.

This table shows the results of a second study among healthy children enrolled in two health maintenance organizations. In this study, children zero through 23 months of age had rates of hospitalization from influenza of 144 to 187 per 100 thousand children. This rate was more than 5 times higher than for healthy children 2 to 4 years of age, and 5 to 17 years of age.

There are several reasons why young children are at increased risk of hospitalization from influenza. The most important is probably because infection with influenza virus at this age represents the first experience with the virus. After the first infection with influenza virus, the child develops immunologic memory to influenza viruses, and subsequent infections with similar viruses produce less severe illness.

For several years, the Advisory Committee on Immunization Practices and the American Academy of Pediatrics have been discussing options to reduce the burden of influenza among young children. Routine annual vaccination of children 6 months and older with high risk medical conditions has been recommended for many years. For the 2002- 2003 influenza season ACIP and AAP have taken the first steps toward the prevention of influenza in ALL children 6 months to 23 months of age.

What is the Advisory Committee on Immunization Practices- recommendation on influenza vaccination of children?

DR. BONNIE WORD:

ACIP has always recognized that were certain children who have high risk medical conditions, who require yearly influenza vaccination. However, more recently ACIP has become aware that there=s another group of children B and these would be healthy children those children less than 2 years of age who have increased rates of complications as well as increased rates of

hospitalization when infected with influenza. As a result, ACIP is now recommending that all children less than 23 months of age or should I say between 6 months and 23 months of age receive influenza vaccine when feasible. So the wording specifically is that for practitioners it is encouraged to administer vaccine to those children between 6 months and 23 months of age when feasible.

What are the obstacles to a recommendation for influenza vaccination all children 6 B 23 months of age?

ACIP anticipates making a full recommendation for administration of influenza vaccine to all children between 6 and 23 months of age within the next three years. However, prior to making this recommendation there are several obstacles that must be overcome. First and foremost is education. Education of not only the health care providers but also the parents. Many individuals on both sides feel that influenza is a viral illness B it-s simply a right of passage. I think once they recognize that there are increased hospitalization rates and complications associated with influenza, particularly in younger children, I think they will begin to look at this from a different perspective. The other thing is that we do have a vaccine that is available B a vaccine that can help prevent and diminish the complications associated with it and I think once that message gets out people are going to be more willing to utilize it. The next thing is just looking at the feasibility and the logistics of administering this vaccine in a certain time period. Unlike most vaccines that practitioners are accustomed to administering, this one will be administered on a seasonable basis. There is a certain time frame- a time window where-s it-s optimal for children to receive it B or should I say all individuals to receive vaccination. That will be something different and something that they-ll have to adjust and get accustomed to within their own practices and find out what-s the best way for this to work within their specific practices. The third thing will be reimbursement issues. You can-t ask a group of practitioners to begin to administer vaccine and not have found ways where they will be adequately reimbursed for their time as well as the administration costs that they will incur.

What other strategies can help prevent influenza in young children?

We spend a great deal of time focusing on children 6 to 23 months of age. However, the group of children who are actually

most vulnerable for influenza, its complications and hospitalizations will be those infants less than 6 months of age. Unfortunately, there is no vaccine available. So the only way we can target those infants and try to prevent infections and complications would be to target their contacts. And this would include all their household contacts, not just their parents, but all their household contacts. As well as administering vaccine to all individuals who have prolonged contact with these children. For example, it may be the individual who is providing daycare services. They may be spending 4 to 6 hours a day with that child. That would be an individual who you would want to immunize.

ATKINSON:

The new ACIP recommendation to encourage influenza vaccination of all children 6 to 23 months of age, when feasible, is only the first step. As Dr. Word mentioned, we expect ACIP and the Academies of Pediatrics and Family Physicians to recommend ROUTINE annual vaccination within the next 3 years. If you provide health care services to children, you should begin thinking about how to integrate annual influenza vaccination into your practice. At the very least, you should be vaccinating children 6 months and older who have underlying medical conditions. This will help acclimate your office to a seasonal vaccine, and get ready for the day when influenza vaccine becomes a part of routine childhood vaccination.

For the 2002-2003 influenza season there will be no changes to groups of children eligible for influenza vaccine under the Vaccines for Children- or VFC- program. Coverage currently includes children 6 months of age and older with high risk medical conditions. But NEXT year- the 2003-2004 influenza season, VFC coverage for influenza vaccine will be extended to healthy children aged 6 to 23 months of age, and children aged 2 to 18 years who are household contacts of children 2 years of age and younger.

As you know, influenza vaccine distribution was delayed during the last 2 influenza seasons. Based on manufacturer's estimates, projected influenza vaccine production for 2002-2003 is between 92 and 97 million doses. This is an increase of 5 to 10 million doses compared to last year. We hope you have already ordered your influenza vaccine for the 2002-2003 season. If you haven't, influenza vaccine is still available for purchase, and you should place your order as soon as possible. Both Aventis Pasteur and Wyeth have informed us that all of their influenza vaccine for the 2002-2003 season has been pre-booked, but their waiting lists remain open. Evans

vaccine is still available from several distributors. Details of influenza vaccine supply and availability, and contact information for manufacturers and distributors is available on the National Immunization Program website. We will give you the address at the end of the program. While you are visiting the website, have a look at our new educational and promotional information for influenza vaccine. For this season there are new flyers describing the timing of influenza vaccination, and myths concerning influenza vaccine. You can download the flyers for your office. They are free.